Final Progress Report for Research Projects Funded by Health Research Grants

Instructions: Please complete all of the items as instructed. Do not delete instructions. Do not leave any items blank; responses must be provided for all items. If your response to an item is "None", please specify "None" as your response. "Not applicable" is not an acceptable response for any of the items. There is no limit to the length of your response to any question. Responses should be single-spaced, no smaller than 12-point type. The report **must be completed using MS Word**. Submitted reports must be Word documents; they should not be converted to pdf format. Questions? Contact Health Research Program staff at 717-783-2548.

1. **Grantee Institution:** Albert Einstein Healthcare Network

2. **Reporting Period (start and end date of grant award period):** 1/1/13-6/30/14

3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Mary Klein, PhD

4. **Grant Contact Person's Telephone Number:** 215-456-7864

5. **Grant SAP Number:** 4100062198

6. **Project Number and Title of Research Project:** #1- Electrophysiologic and Behavioral Evidence of Consciousness: a Longitudinal Analysis

7. **Start and End Date of Research Project: 1/1/13-6/30/14**

8. **Name of Principal Investigator for the Research Project:** John Whyte, MD, PhD

9. **Research Project Expenses**.

   9(A) Please provide the total amount of health research grant funds spent on this project for the entire duration of the grant, including indirect costs and any interest earned that was spent:

   $ 30,928.70

   9(B) Provide the last names (include first initial if multiple individuals with the same last name are listed) of **all** persons who worked on this research project and were supported with health research funds. Include position titles (Principal Investigator, Graduate Assistant, Post-doctoral Fellow, etc.), percent of effort on project and total health research funds expended for the position. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name, First Name	Position Title	% of Effort on Project	Cost

9(C) Provide the names of **all** persons who worked on this research project, but who *were not* supported with health research funds. Include position titles (Research Assistant, Administrative Assistant, etc.) and percent of effort on project. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name, First Name	Position Title	% of Effort on Project
Whyte, John	PI	5%
Day, Kristin	Co-PI	100%
Kim, Junghoon	Consultant	3%

9(D) Provide a list of **all** scientific equipment purchased as part of this research grant, a short description of the value (benefit) derived by the institution from this equipment, and the cost of the equipment.

Type of Scientific Equipment	Value Derived	Cost
BioSemi ActiveTwo EEG system (a portion of the total system purchased with award funds)	Initiated new field of electrophysiology research in TBI at MRRI/MossRehab	$12,000
Additional ActiveTwo EEG cap	Same as above	$1,477.66

10. Co-funding of Research Project during Health Research Grant Award Period. Did this research project receive funding from any other source <u>during the project period</u> when it was supported by the health research grant?

Yes___ x _____ No_____

If yes, please indicate the source and amount of other funds:
Moss Rehabilitation Research Institute (internal funds), Total award: $12,500. A portion of the budget included costs for additional consultants at outside institutions for both this project as well as another ongoing project.

11. Leveraging of Additional Funds

11(A) <u>As a result</u> of the health research funds provided for this research project, were you able to apply for and/or obtain funding from other sources <u>to continue or expand the research</u>?

Yes____x_____   No_____

If yes, please list the applications submitted (column A), the funding agency (National Institutes of Health—NIH, or other source in column B), the month and year when the application was submitted (column C), and the amount of funds requested (column D). If you have received a notice that the grant will be funded, please indicate the amount of funds to be awarded (column E). If the grant was not funded, insert "not funded" in column E.

Do not include funding from your own institution or from CURE (tobacco settlement funds). Do not include grants submitted prior to the start date of the grant as shown in Question 2. If you list grants submitted within 1-6 months of the start date of this grant, add a statement below the table indicating how the data/results from this project were used to secure that grant.

A. Title of research project on grant application	B. Funding agency (check those that apply)	C. Month and Year Submitted	D. Amount of funds requested:	E. Amount of funds to be awarded:
Examination of resting state EEG in persons with severe brain injury: neural mechanisms for the recovery of consciousness	☐NIH ☐ Other federal (specify:_____ _____) ☒ Nonfederal source (specify: Arcadia University)	3/2014	$ 3,000	$ 3,000
	☐NIH ☐ Other federal (specify:_____ _____) ☐ Nonfederal source (specify: _____)		$	$

11(B) Are you planning to apply for additional funding in the future to continue or expand the research?

Yes_____x_____   No_____

If yes, please describe your plans:

We plan to enroll a few more subjects using remaining internal pilot funds in order to generate sufficient preliminary data to support a larger grant application from a federal research agency to continue with our longitudinal analysis of recovery of consciousness.

12. **Future of Research Project.** What are the future plans for this research project?

As noted previously, this is a multi-phase project. The first phase involved laboratory set up, technical debugging, and initial development of analytic strategies, which has largely been achieved. The next phase will involve validation of the EEG and accelerometry measures against other indicators of consciousness. The final phase will involve use of these techniques to explore the recovery of consciousness as assessed behaviorally and electrophysiologically and an examination of the reasons for mismatches that are identified.

13. **New Investigator Training and Development**. Did students participate in project supported internships or graduate or post-graduate training for at least one semester or one summer?

Yes_____x_____   No_____

If yes, how many students? Please specify in the tables below:

	Undergraduate	Masters	Pre-doc	Post-doc
Male				
Female			1	1
Unknown				
Total			**1**	**1**

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic			1	1
Unknown				
Total			**1**	**1**

	Undergraduate	Masters	Pre-doc	Post-doc
White			1	1
Black				
Asian				
Other				
Unknown				
Total			**1**	**1**

14. Recruitment of Out-of–State Researchers. Did you bring researchers into Pennsylvania to carry out this research project?

Yes____x_____   No_____

If yes, please list the name and degree of each researcher and his/her previous affiliation:
Kristin V. Day, PhD, MPT, NCS: affiliated with Cardinal Hill Rehabilitation Hospital, Lexington, KY prior to Moss Rehabilitation Research Institute and Arcadia University in Pennsylvania.

15. Impact on Research Capacity and Quality. Did the health research project enhance the quality and/or capacity of research at your institution?

Yes_____x____   No_____

If yes, describe how improvements in infrastructure, the addition of new investigators, and other resources have led to more and better research.

These funds helped set up a brain electrophysiology lab and provide initial experience in its use. This lab is now available for ongoing research on recovery from disorders of consciousness as well as potentially other EEG-based study designs.

16. Collaboration, business and community involvement.

16(A) Did the health research funds lead to collaboration with research partners outside of your institution (e.g., entire university, entire hospital system)?

Yes____x_____   No_____

If yes, please describe the collaborations:

Approximately nine months into this project, we initiated collaborations with physician scientists, who have expertise in specialized quantitative EEG applications for Disorders of Consciousness, at Weill Cornell Medical College and Burke Rehabilitation Hospital in New York.

16(B) Did the research project result in commercial development of any research products?

Yes_____   No_____x_____

If yes, please describe commercial development activities that resulted from the research project:

16(C) Did the research lead to new involvement with the community?

Yes_____   No_____x_____

If yes, please describe involvement with community groups that resulted from the research project:

17. Progress in Achieving Research Goals, Objectives and Aims.
List the project goals, objectives and specific aims (as contained in the grant agreement). Summarize the progress made in achieving these goals, objectives and aims <u>for the period that the project was funded (i.e., from project start date through end date).</u> Indicate whether or not each goal/objective/aim was achieved; if something was not achieved, note the reasons why. Describe the methods used. If changes were made to the research goals/objectives/aims, methods, design or timeline since the original grant application was submitted, please describe the changes. <u>Provide detailed results of the project.</u> Include evidence of the data that was generated and analyzed, and provide tables, graphs, and figures of the data. List published abstracts, poster presentations and scientific meeting presentations at the end of the summary of progress; peer-reviewed publications should be listed under item 20.

This response should be a <u>DETAILED</u> report of the methods and findings. It is not sufficient to state that the work was completed. Insufficient information may result in an unfavorable performance review, which may jeopardize future funding. If research findings are pending publication you must still include enough detail for the expert peer reviewers to evaluate the progress during the course of the project.

Health research grants funded under the Tobacco Settlement Act will be evaluated via a performance review by an expert panel of researchers and clinicians who will assess project work using this Final Progress Report, all project Annual Reports and the project's strategic plan. After the final performance review of each project is complete, approximately 12-16 months after the end of the grant, this Final Progress Report, as well as the Final Performance Review Report containing the comments of the expert review panel, and the grantee's written response to the Final Performance Review Report, will be posted on the CURE Web site.

There is no limit to the length of your response. Responses must be single-spaced below, no smaller than 12-point type. If you cut and paste text from a publication, be sure symbols print properly, e.g., the Greek symbol for alpha (α) and beta (ß) should not print as boxes ($\Box$) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

<u>**Specific Aims and Progress**</u>

The aims for this project were proposed as follows. A summary of the progress made toward each aim is described below the respective aim.

Specific Aim #1: (Operational) Debug the data acquisition protocol, hardware, and software systems to ensure accurate collection of relevant data, and refine the machine learning data analysis algorithms that characterize the accuracy of both EEG and behavioral motion data.

Progress: Overall, this operational aim was achieved. Using a combination of funds from this award and institutional funds, we acquired a brand new BioSemi ActiveTwo EEG system with custom-designed accelerometers and developed a mobile laboratory cart for ease of data collection in a hospital environment. Although the equipment delivery was delayed approximately 4 months into the award period, we successfully assembled the lab, synchronized the EEG and accelerometers including

the implementation of event codes, learned the acquisition and analysis software systems, developed four auditory paradigms, and learned what constitutes and how to acquire quality data. Healthy controls were tested as stated in our original proposal, but as the project developed, we decided to modify our protocol and test persons with brain injury, who were fully conscious and able to follow simple commands; this modification was made to ensure that any failure to detect consciousness in patients with disorders of consciousness (DoCs) was truly due to their mental state rather than their brain injury more generally. We had proposed to classify EEG data from individual trials as "move" or "hold still" trials based on a machine classifier. However, early in the project period, this method was criticized in the literature as being based on faulty statistical assumptions. Thus, we chose to implement different EEG analyses to classify accuracy, based on methods developed and published by our consultants. We developed parallel classification methods for the accelerometry analysis. These approaches are discussed below in the methodology.

**Note regarding recruitment: This refinement phase of the study was the rate-limiting factor in our recruitment goals for the subsequent longitudinal phase (Specific Aim #2). Although part of Aim #1 was to "debug" the hardware and software systems and acquire control data, the other part was to refine our analyses prior to proceeding with the longitudinal phase of the study. As a result of our new consultant collaboration nine months into the award period, and needed changes in our analytic approach, the second phase of the study was delayed.

Specific Aim #2: Obtain preliminary data on the test-retest reliability and pattern of longitudinal recovery of data in both domains to support power and sample size calculations for an externally funded project.

Progress: This aim is ongoing as we continue to enroll patients with DoCs. We have discovered the challenges of using EEG caps with this acute/subacute patient population (e.g., concave/convex hemicraniectomy sites, diaphoresis) and are continually addressing ways to improve data quality. Each patient case is unique. Despite these challenges, we have been able to collect longitudinal data, three times weekly, from three individuals with DoCs. A fourth patient was admitted to the Responsiveness Program during this phase of the study and his parents were approached for consent. They declined participation because of time involvement. They desired that the patient have time to rest between therapies rather than participate in the study.

Specific Aim #3: (Exploratory) Using physical examination data about sensory and motor deficits and imaging data related to focal lesions, develop hypotheses about the source of discrepancies between EEG and behavioral evidence for consciousness.

Progress: Because we are continuing to collect data from patients with DoCs in accordance with Specific Aim #2 and due to the extended time required to develop and change analysis techniques, we were unable to address Specific Aim #3 within the project award period.

Review of methodology

Participants
All participants were age 18 and older. For Aim #1, they were healthy individuals and patients with severe BI who were fully conscious and able to follow simple commands well. For Aim #2, these

individuals were admitted to the Drucker Brain Injury Center's Responsiveness Program in a vegetative or minimally conscious state, regardless of etiology.

Procedure
For Aim #1, individuals participated in up to 3 individual sessions of EEG and accelerometry data collection only. However, for Aim #2 (longitudinal phase), participants with DoCs were tested three times weekly, once with the Coma Recovery Scale-Revised and twice with EEG and accelerometry, for the duration of their time in the Responsiveness Program.

EEG and accelerometer sessions involved instrumentation of participants with an EEG cap with gel, 128 cap electrodes, reference and electrooculogram electrodes, and accelerometers attached to the dorsum of the hands. A minute of resting baseline data was collected first. Then an auditory stimulation paradigm randomly instructed participants to either "move hands" or "hold still" for 60 total trials (30 for each command). The interstimulus interval was 10 seconds.

Processing and Analysis
EEG: Pre-processing steps included manual rejection of data segments with obvious motion artifacts, removal of 60Hz line noise, and removal of eye movement and electromyographic artifact with Independent Component Analysis. Next, a Laplacian montage and a multitaper Fourier transform were applied. Finally, a Two Group Test (TGT) was conducted for 26 channels of data along the motor strip (Figure 1) from 4 to 24 Hz (frequencies within which we would anticipate differences between conditions) to determine if significant differences existed among electrical signals when patients were asked to "move hands" versus "hold still." ($p<.05$) Note that this analysis asks whether, in the entire EEG dataset, there is evidence for a difference between "move hands" and "hold still" trials, but it does not classify the accuracy of response on each trial. We are currently consulting with a local biostatistician to explore development of a reliable accuracy metric that is based on individual trials.
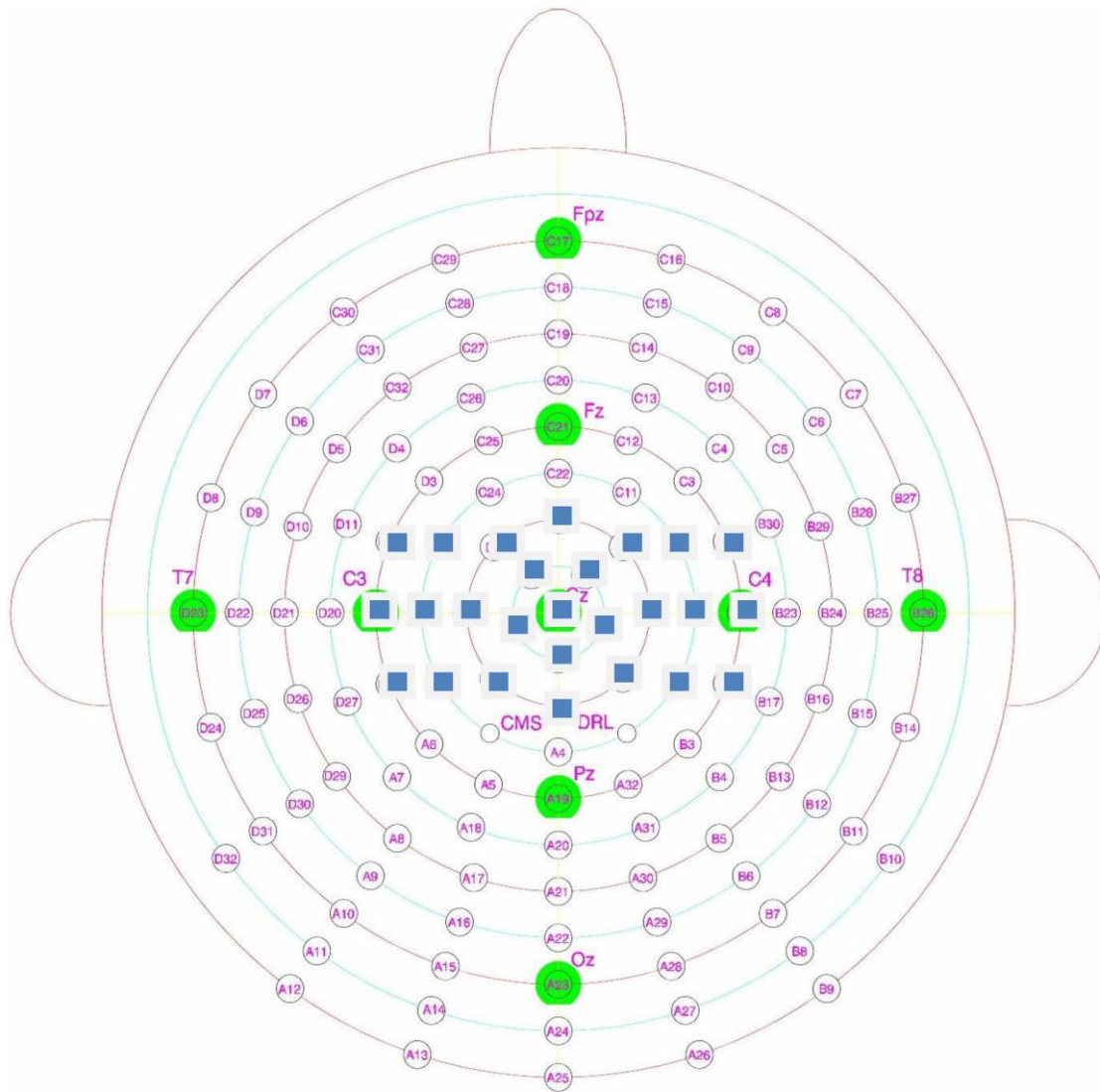
Figure 1. 2D scalp map of the BioSemi ActiveTwo EEG cap. Blue squares overlie those electrode channels used for analysis. For reference, the green circles highlight channels typically involved in the international 10-20 EEG configuration.

Accelerometry: 3D accelerations from bilateral hands were extracted into epochs and grouped by command type. The mean of 3D accelerations from each trial (excluding the first second after command delivery) within each command type was calculated. These trials were ordered with respect to magnitude of acceleration such that if the subject were perfectly accurate, the 30 trials with the largest acceleration should all be "move hands" trials and the 30 with the smallest acceleration should all be "hold still" trials. Violations of this ordering can be used to tabulate accuracy on an individual trial basis. The Mann-Whitney U test was performed to test the statistical significance of the difference in acceleration between "move hands" and "hold still" trials ($p<.05$).

<u>Results</u>

Given the heterogeneity in the patient population with BI and the fact that each case must be analyzed individually, these results provide representative data from the various participant groups tested in the refinement and longitudinal phases. Additionally, because we are exploring new, complementary analyses to look at each trial during a session (versus all trials averaged together) and are continuing to collect data from persons with DoCs beyond the funded project period in order to increase sample size, we are refraining from drawing definitive conclusions about the degree of consciousness for persons with DoCs studied thus far. Each case presented here has EEG and acceleration data grouped together.

EEG
For all spectrograms below, data represent the difference between the average of all "move hands" and all "hold still" trials. The x-axis denotes time in seconds. The first second is the time in which the command was presented followed by the response interval. Along the y-axis are the individual electrodes (e.g., A1, B19) along the motor strip bilaterally as well as the frequency bands (5 to 25Hz). On the far right, the color spectra quantify power changes represented by color bands in the spectrogram (-10 to 10 dB). Non-significant power changes have been made translucent, while significant changes have prominent color bands ($p<.05$). Of those changes that are significant, we aimed to observe concentrated patterns of decreased power (blue bands) throughout several electrode channels during the response interval (e.g. Figures 2a, 3a) rather than bands scattered in a few channels for brief periods (e.g. Figures 4a, 5a).

Accelerations
Accuracy of movement or lack of movement for command conditions is presented below in dot density graphs. The x-axes show acceleration values. We aimed to observe tight data clusters with true hand movement occurring when the "move" command was given (high values) and no hand movement when the "hold still" command was given (values around zero). Figure 2b for a control participant displays this separation with 100% accuracy.
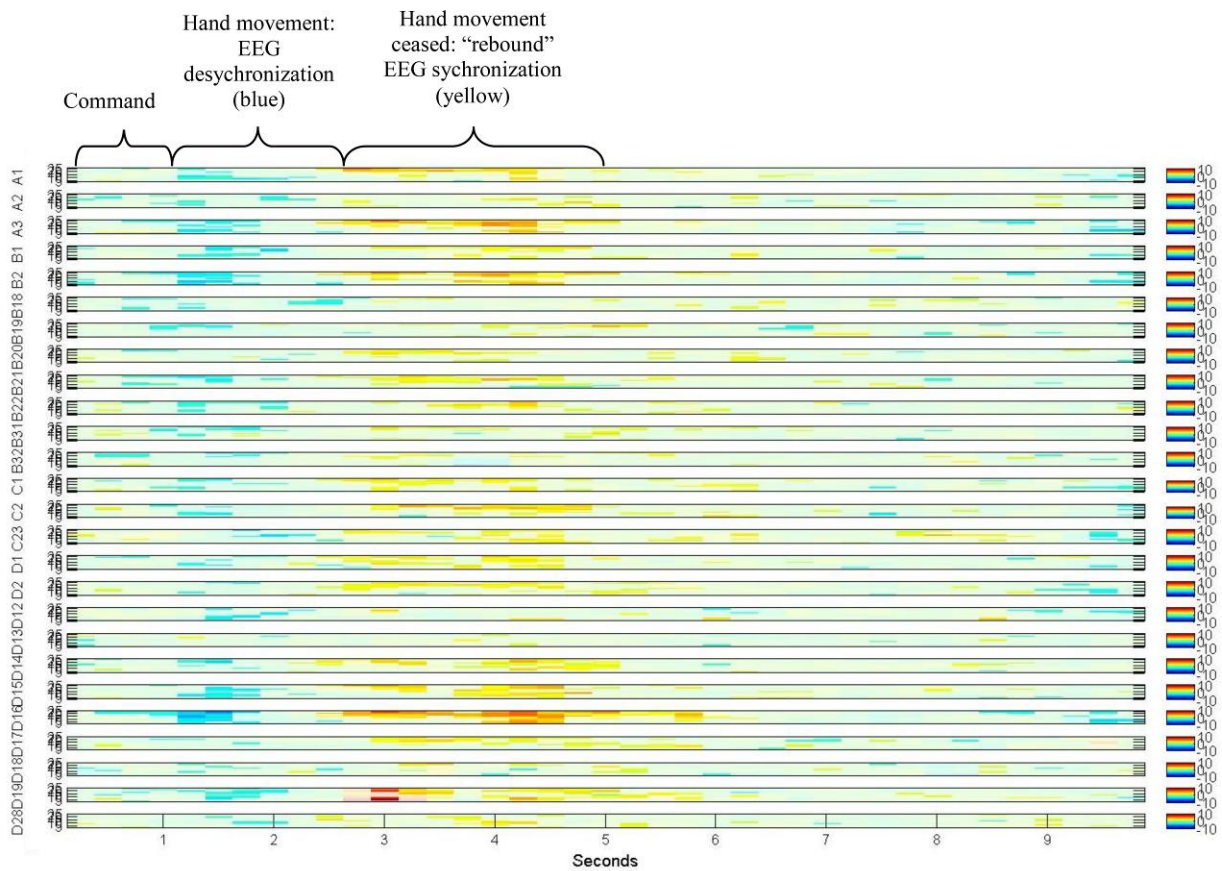
Figure 2a. Spectrogram for 23 year old female control participant. This individual moved bilateral hands briefly over 1-2 seconds immediately after the command.
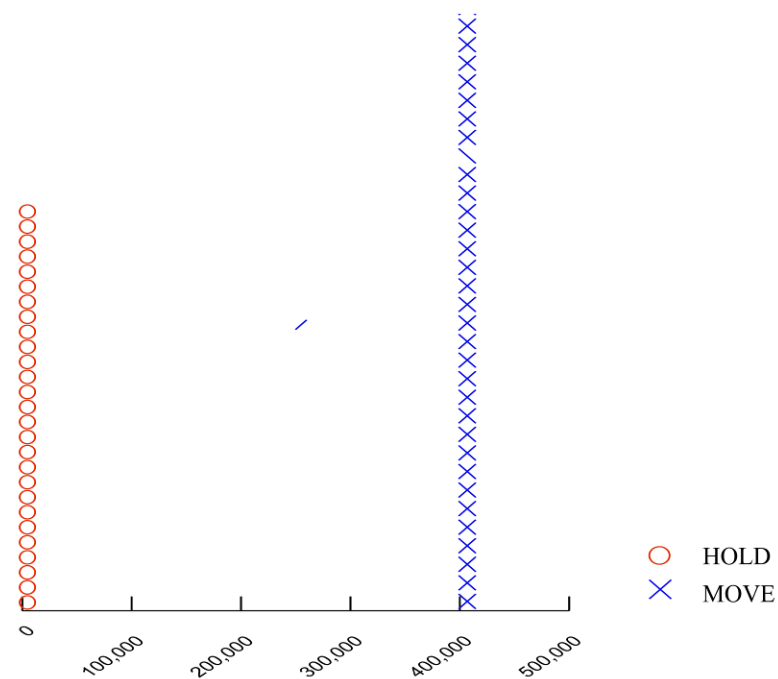

Figure 2b. Acceleration values for the control participant. Note the perfect separation of data for the two conditions ($p<0.001$).
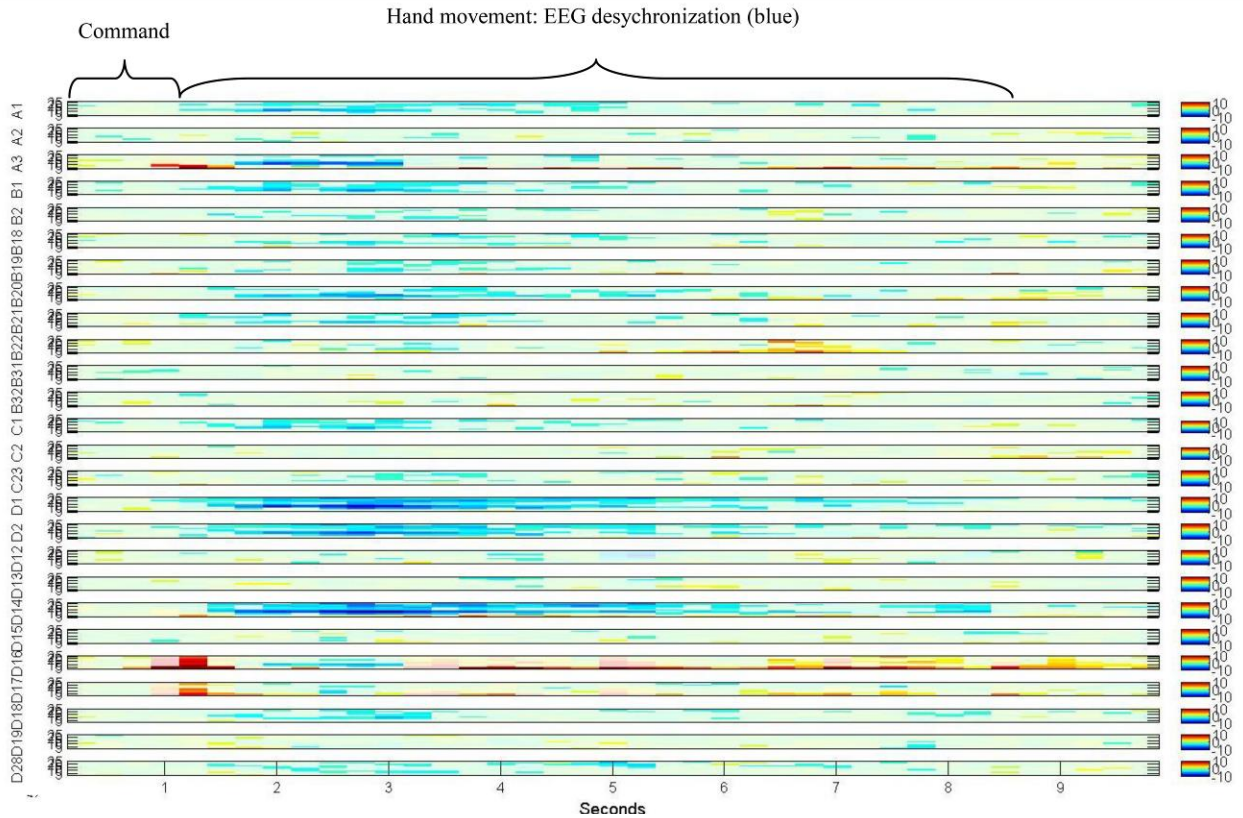
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Figure 3a. Spectrogram for 58 year old female with BI, fully conscious, and able to follow simple commands. This individual moved both hands continuously throughout the "move hands" trials.
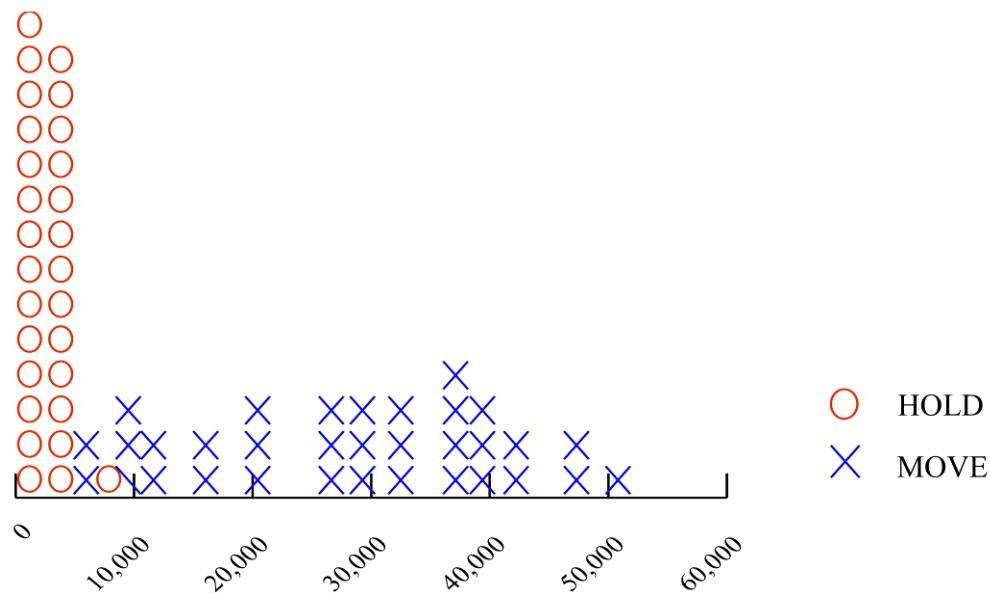

Figure 3b. Acceleration values for participant with BI. A definitive separation of conditions is observed ($p<0.001$), but greater variability is exhibited within accelerations for the move condition compared to the control participant. Some of the lower values approximate or overlap those in the hold condition.
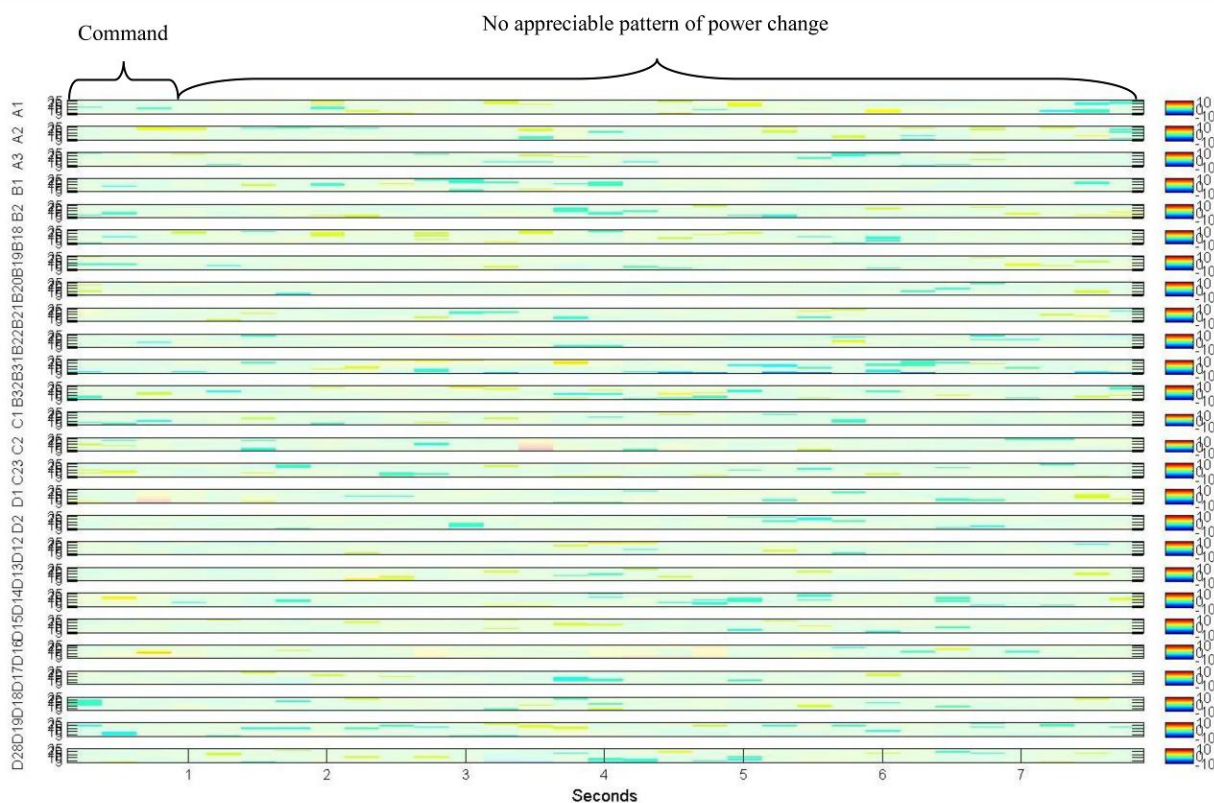
Figure 4a. Spectrogram for 34 year old female clinically diagnosed in vegetative state on CRS-R. No active hand movement.
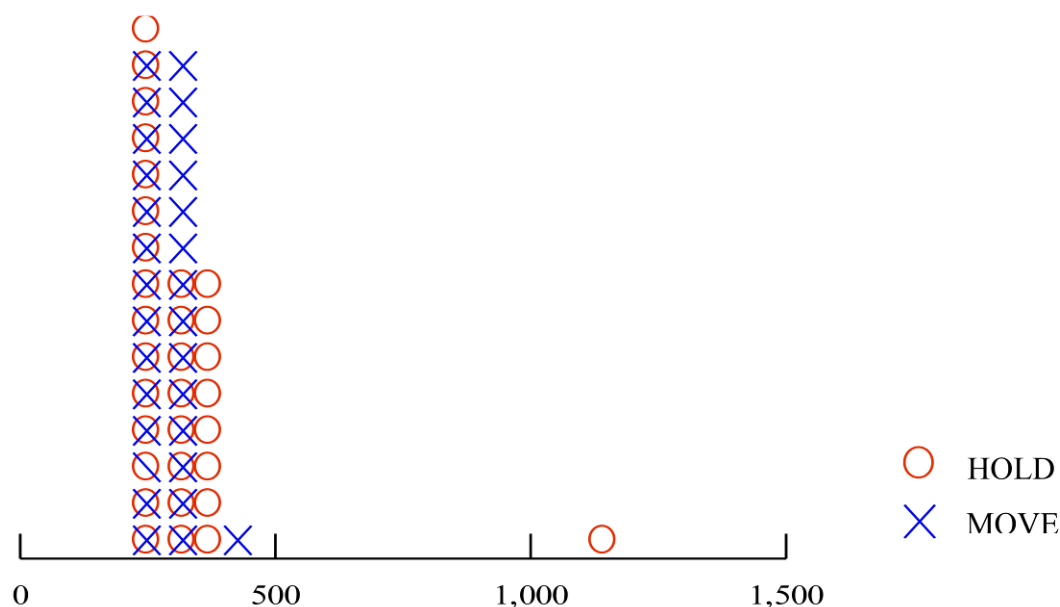

Figure 4b. Acceleration values for participant diagnosed in vegetative state. Zero separation of data is detected ($p=0.942$). Note the small scale on the x-axis relative to those for the control participant (Fig. 2b) and fully conscious participant with BI (Fig. 3b). Acceleration values are minimally above zero due to increased muscle tone in the upper extremities.

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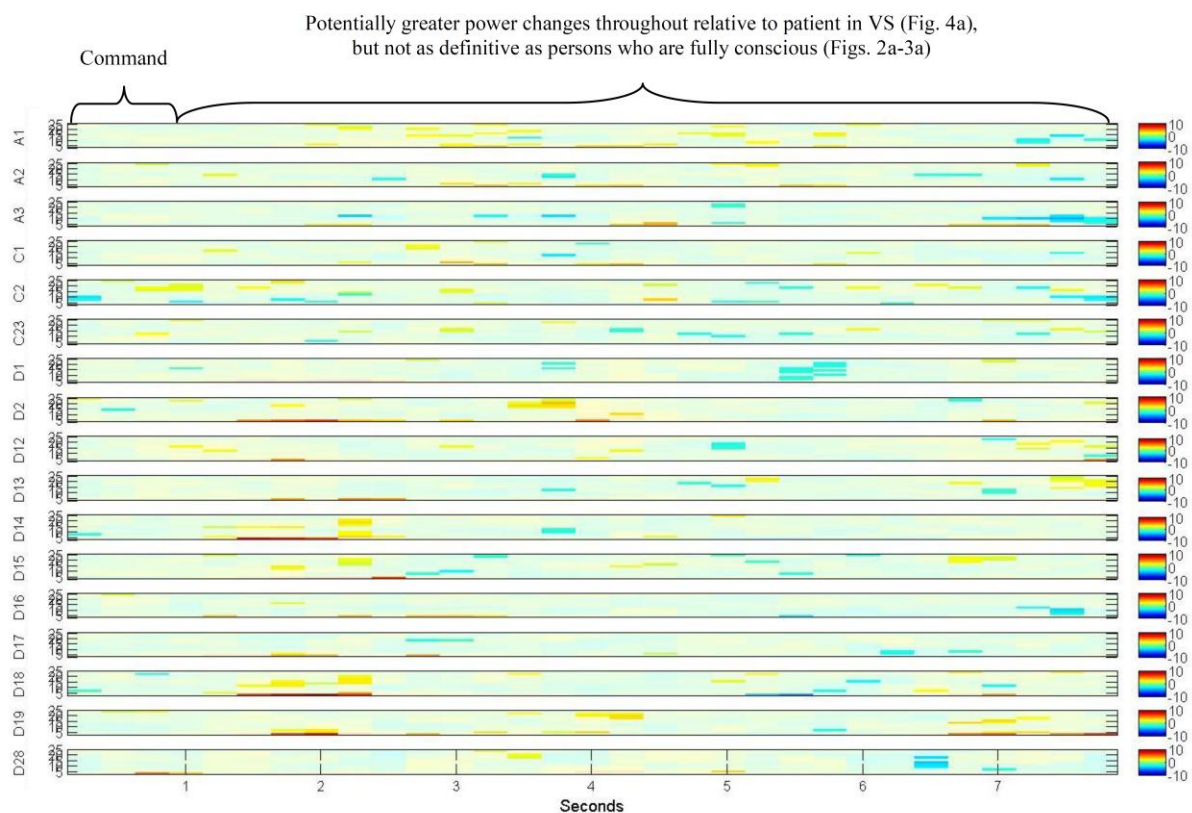Figure 5a. Spectrogram for 19 year old male clinically diagnosed in minimally conscious state on CRS-R (via command following with eye movement). No active hand movement. A reduced number of electrodes is represented due to the extensive right-sided hemicraniectomy surgical site.
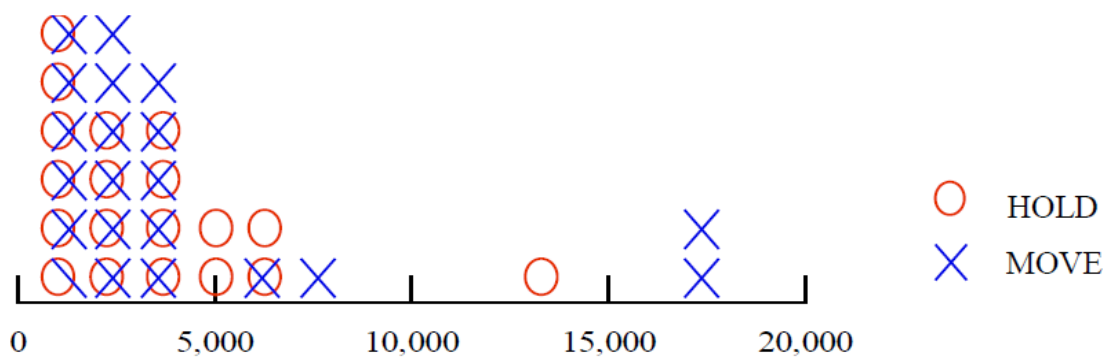

Figure 5b. Acceleration values for participant diagnosed in minimally conscious state. Data lacks separation overall (p=0.946).

<u>**Published abstracts/Scientific meeting presentations**</u>

Day, KV, Whyte, J. Development of an Electrophysiologic and Behavioral Methodology to Assess Consciousness after Severe Brain Injury. Platform Presentation. American Physical Therapy Association Combined Sections Meeting (Neurology Section) February 2014.

Day, KV, Whyte, J. Quantifying command following in disorders of consciousness after brain injury: a novel methodology using accelerometry. Under Review for Platform Presentation at American Physical Therapy Association Combined Sections Meeting (Neurology Section) February 2015.

18. **Extent of Clinical Activities Initiated and Completed**. Items 18(A) and 18(B) should be completed for all research projects.   If the project was restricted to secondary analysis of clinical data or data analysis of clinical research, then responses to 18(A) and 18(B) should be "No."

> 18(A) Did you initiate a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?
> ___x___Yes
> _____No

> 18(B) Did you complete a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?
> _____Yes
> ___x___No

If "Yes" to either 18(A) or 18(B), items 18(C) – (F) must also be completed. (Do NOT complete 18(C-F) if 18(A) and 18(B) are both "No.")

> 18(C) How many hospital and health care professionals were involved in the research project?
> ___2___Number of hospital and health care professionals involved in the research project

> 18(D) How many subjects were included in the study compared to targeted goals?

> ___30___Number of subjects originally targeted to be included in the study
> ____9__Number of subjects enrolled in the study

> **Note**: Studies that fall dramatically short on recruitment are encouraged to provide the details of their recruitment efforts in Item 17, Progress in Achieving Research Goals, Objectives and Aims. For example, the number of eligible subjects approached, the number that refused to participate and the reasons for refusal. Without this information it is difficult to discern whether eligibility criteria were too restrictive or the study simply did not appeal to subjects.

> **See Item #17, Specific Aim #1, "Progress" for further details**

18(E) How many subjects were enrolled in the study by gender, ethnicity and race?

Gender:
___1___Males
___8___Females
_____Unknown

Ethnicity:
___1___Latinos or Hispanics
___8___Not Latinos or Hispanics
_____Unknown

Race:
_____American Indian or Alaska Native
_____Asian
_____Blacks or African American
_____Native Hawaiian or Other Pacific Islander
___9__White
_____Other, specify:_____
_____Unknown

18(F) Where was the research study conducted? (List the county where the research study was conducted. If the treatment, prevention and diagnostic tests were offered in more than one county, list all of the counties where the research study was conducted.)

Montgomery

19. **Human Embryonic Stem Cell Research.** Item 19(A) should be completed for all research projects. If the research project involved human embryonic stem cells, items 19(B) and 19(C) must also be completed.

19(A) Did this project involve, in any capacity, human embryonic stem cells?
_____Yes
___x___ No

19(B) Were these stem cell lines NIH-approved lines that were derived outside of Pennsylvania?
_____Yes
_____ No

19(C) Please describe how this project involved human embryonic stem cells:

20. **Articles Submitted to Peer-Reviewed Publications**.

20(A) Identify all publications that resulted from the research performed during the funding period and that have been submitted to peer-reviewed publications. Do not list journal abstracts or presentations

at professional meetings; abstract and meeting presentations should be listed at the end of item 17. **Include only those publications that acknowledge the Pennsylvania Department of Health as a funding source** (as required in the grant agreement). List the title of the journal article, the authors, the name of the peer-reviewed publication, the month and year when it was submitted, and the status of publication (submitted for publication, accepted for publication or published.). Submit an electronic copy of each publication or paper submitted for publication, listed in the table, in a PDF version 5.0.5 (or greater) format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, and an abbreviated title of the publication. For example, if you submit two publications for Smith (PI for Project 01), one publication for Zhang (PI for Project 03), and one publication for Bates (PI for Project 04), the filenames would be:

  Project 01 – Smith – Three cases of isolated
  Project 01 – Smith – Investigation of NEB1 deletions
  Project 03 – Zhang – Molecular profiling of aromatase
  Project 04 – Bates – Neonatal intensive care
If the publication is not available electronically, provide 5 paper copies of the publication.

Note: The grant agreement requires that recipients acknowledge the Pennsylvania Department of Health funding in all publications. Please ensure that all publications listed acknowledge the Department of Health funding. If a publication does not acknowledge the funding from the Commonwealth, do not list the publication.

Title of Journal Article:	Authors:	Name of Peer-reviewed Publication:	Month and Year Submitted:	Publication Status (check appropriate box below):
1.				☐Submitted ☐Accepted ☐Published
2.				☐Submitted ☐Accepted ☐Published
3.				☐Submitted ☐Accepted ☐Published

20(B) Based on this project, are you planning to submit articles to peer-reviewed publications in the future?

Yes____x_____   No_____

If yes, please describe your plans:

With the addition of more participants with DoCs over the next several months as well as further development of an individual-trial statistical method, we will be in a position to submit a publication based on pilot data from this project.

21. Changes in Outcome, Impact and Effectiveness Attributable to the Research Project. Describe the outcome, impact, and effectiveness of the research project by summarizing its impact on the incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of outcome, impact or effectiveness of the research project. If there were no changes, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

At this time the major impact of this project has been on the development of a fully functional, mobile electrophysiology lab (with complementary motion equipment) at Moss Rehabilitation Research Institute and MossRehab. This lab will allow for not only this project, but continuation of a sustainable line of research.

22. Major Discoveries, New Drugs, and New Approaches for Prevention Diagnosis and Treatment. Describe major discoveries, new drugs, and new approaches for prevention, diagnosis and treatment that are attributable to the completed research project. If there were no major discoveries, drugs or approaches, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

None.

23. Inventions, Patents and Commercial Development Opportunities.

23(A) Were any inventions, which may be patentable or otherwise protectable under Title 35 of the United States Code, conceived or first actually reduced to practice in the performance of work under this health research grant? Yes_____   No____x____

If "Yes" to 23(A), complete items a – g below for each invention. (Do NOT complete items a - g if 23(A) is "No.")

    a. Title of Invention:

    b. Name of Inventor(s):

    c. Technical Description of Invention (describe nature, purpose, operation and physical, chemical, biological or electrical characteristics of the invention):

    d. Was a patent filed for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
       Yes_____   No____

       If yes, indicate date patent was filed:

e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____   No____
If yes, indicate number of patent, title and date issued:
Patent number:
Title of patent:
Date issued:

f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes_____   No____

If yes, how many licenses were granted?_____

g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes_   No____

If yes, describe the commercial development activities:

23(B) Based on the results of this project, are you planning to file for any licenses or patents, or undertake any commercial development opportunities in the future?

Yes_____   No_____x_____

If yes, please describe your plans:

24. Key Investigator Qualifications. Briefly describe the education, research interests and experience and professional commitments of the Principal Investigator and all other key investigators. In place of narrative you may insert the NIH biosketch form here; however, please limit each biosketch to 1-2 pages. *For Nonformula grants only – include information for only those key investigators whose biosketches were not included in the original grant application.*

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
John Whyte, MD, PhD	Director
eRA COMMONS USER NAME (credential, e.g., agency login) JWHYTEMRRI	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Swarthmore College	BA	1974	Biology
University of Pennsylvania	MD	1978	Medicine
University of Pennsylvania	PhD	1981	Experimental Psychology
University of Minnesota	Residency	1984	PM&R
Tufts University School of Medicine	Fellowship	1985	Neurotrauma

A. Personal Statement

As a physician specializing in traumatic brain injury (TBI) rehabilitation and a cognitive psychologist, I have spent many years caring for and studying individuals with severe brain injury and disorders of consciousness (DOC). I have developed specialized clinical programs, improved means of assessment of consciousness, and have studied the impact of several treatments.

B. Positions and Honors

Positions and Employment
9/85-9/89	Director of Research, Associate Director of Rehabilitation Medicine, Greenery Rehabilitation and Skilled Nursing Center, Boston
9/85-9/89	Assistant Physiatrist, New England Medicine Center Hospitals, Boston
9/85-9/89	Assistant Professor of Rehabilitation Medicine, Tufts University School of Medicine, Boston
1/90-1/98	Associate Professor, Department of Physical Medicine and Rehabilitation. Temple Health Sciences Center, Philadelphia
9/89-present	Attending Physiatrist, Drucker Brain Injury Center, MossRehab, Philadelphia
9/89-present	Staff Physiatrist, Moss Practic Plan, Inc., Philadelphia
7/92-present	Director, Moss Rehabilitation Research Institute, Philadelphia
1995-present	Director, Responsiveness Program, Drucker Brain Injury Center, MossRehab
1/98-2000	Professor, Department of Physical Medicine and Rehabilitation. Temple Health Sciences Center, Philadelphia
2000-present	Professor, Department of Rehabilitation Medicine, Jefferson Medical College, Thomas Jefferson University
2000-present	Adjunct Professor, Department of Physical Medicine and Rehabilitation, Temple Health Sciences Center

Other Experience
2000-2004	National Advisory Board on Medical Rehabilitation Research (NABMRR), National Institute of Child Health and Human Development (NICHD)
	• 2003-2004 Chair
2005 – 2006	Committee on Disability in America, Institute of Medicine
2011	Committee on Cognitive Rehabilitation Therapy for Traumatic Brain Injury, Institute of Medicine

Honors
2002	William Fields Caveness Award, Brain Injury Association of America

2005	Brain Injury Association of Pennsylvania, Inc. Pioneer in Brain Injury Award for Outstanding Research
2005	Distinguished Member Award, American Congress of Rehabilitation Medicine
2007	American Congress of Rehabilitation Medicine John Stanley Coulter Lectureship Award
2008	Robert L. Moody Prize for Distinguished Initiatives in Brain Injury Research and Rehabilitation
2010	Distinguished Academician, Association of Academic Physiatrists
2012	Joel A. DeLisa, MD Award for Excellence in Research and Education in the Field of Physical Medicine & Rehabilitation

C. Selected Peer-reviewed Publications (selected from > 120 peer reviewed publications)

Whyte J, Hart T, Bode RK, Malec JF: The Moss attention rating scale (MARS)© for traumatic brain injury: Initial psychometric assessment. Arch Phys Med Rehabil 84(2):268-276, 2003 PMID: 12601660

Whyte J, Hart T, Vaccaro M, Grieb-Neff P, Risser A, Polansky M, Coslett HB: The effects of methylphenidate on attention deficits after traumatic brain injury: A multi-dimensional randomized controlled trial. American Journal of Physical Medicine and Rehabilitation, 83(6):401-420, 2004 PMID: 15166683

Whyte J, Hart T, Ellis C, Chervoneva I: The Moss Attention Rating Scale for traumatic brain injury: Further explorations of reliability and sensitivity to change. Arch Phys Med Rehabil, 89:966-973, 2008 PMID: 18452747

Hart T, Whyte J, Ellis C, Chervoneva I: Construct validity of an Attention Rating Scale for traumatic brain injury. Neuropsychology, 23(6):729-735, 2009 PMID: 19899831

Whyte J, Myers R: Incidence of clinically significant responses to Zolpidem among patients with disorders of consciousness: A preliminary placebo controlled trial. American Journal of Physical Medicine and Rehabilitation, 88(5):410-418, 2009

Giacino JT*, Whyte J*, Bagiella E, Kalmar K, Childs N, Khademi A, Eifert M, Long D, Katz DI, Cho S, Yablon SA, Luther M, Hammond FM, Nordenbo A, Novak P, Mercer W, Maurer-Karattup, P, Sherer M: Placebo-controlled trial of amantadine for severe traumatic brain injury. New England Journal of Medicine, 366(9): 819-26, 2012 PMID: 22375973 [* co-first authors]

Whyte J, Barrett AM. Advancing the evidence base of rehabilitation treatments: A developmental approach. Arch Phys Med Rehabil, 93(Suppl 2) S101-S110, 2012 PMID:22683206

Whyte J, Nordenbo AM, Kalmar K, Merges B, Bagiella E, Chang H, Yablon S, Cho S, Hammond F, Khademi A, Giacino J: Medical Complications During Inpatient Rehabilitation Among Patients with Traumatic Disorders of Consciousness. Arch Phys Med Rehabil Medicine (in press)

Whyte J, et al: Functional outcomes in traumatic disorders of consciousness; 5-year outcomes from the NIDRR Traumatic Brain Injury Model Systems. Arch Phys Med Rehabil (in press)

Whyte J, Nakase-Richardson R, Hammond FM, McNamee S, Giacino JT, Kalmar K, Greenwald B, Yablon SA, Horn LJ: Functional outcomes in traumatic disorders or consciousness: 5-year outcomes from the NIDRR traumatic brain injury model systems. Arch Phys Med Rehabil (in press)

Nakase-Richardson R, Tran J, Cifu D, Barnett SD, Horn LJ, Greenwald BD, Brunner RC, Whyte J, Hammond FM, Yablon SA, Giacino JT: Do rehospitalization rates differ among severity levels in the NIDRR Traumatic Brain Injury Model Systems Program? 2013 [Epub ahead of print] PMID:23770278

Whyte J. The contributions of treatment theory and enablement theory to rehabilitation research and practice. Arch Phys Med Rehabil. (in press)

Chatelle C, Thibaut A, Whyte J, DeVal MD, Laureys S, Schnakers C: Pain issues in disorders of consciousness. Brain Injury, (accepted)

D.   Research Support

Current Research Support as Principal Investigator

1T32HD071844-01A1   Wjyte (PI)   5/13/2013-4/30/2018
Postdoctoral Training in Translational Neurorehabilitation Research
The major goal of this project is to train postdoctoral fellows, recruited from basic science and clinical disciplines using a mixture of didactic and hands-on training methods.

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Kristin Vamvas Day, PhD, MPT, NCS	POSITION TITLE Assistant Professor of Physical Therapy
eRA COMMONS USER NAME (credential, e.g., agency login)	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Ohio University, Athens, OH	BS	2000	Biological Sciences
Ohio University, Athens, OH	MPT	2002	Physical Therapy
University of Florida, Gainesville, FL	PhD	2010	Rehabilitation Science
Moss Rehabilitation Research Institute, Elkins Park, PA	Post-doc	2014	Electrophysiology/ Disorders of Consciousness

A. Personal Statement

As a researcher and neurologic clinical specialist in physical therapy with a passion for accelerating recovery of function in persons post-neurologic injury, I have experience and a continued interest in understanding and exposing neural mechanisms for recovery across multiple domains including consciousness and motor control.

B. Positions and Honors

1998-1999	**Assistant Exercise Physiologist**, Department of Biological Sciences, Ohio University, Athens, OH
2000-2001	**Research Coordinator**, College of Osteopathic Medicine, Ohio University, Athens, OH
2002-2004	**Staff Physical Therapist**, Adult inpatient rehab/acute care, Greenville Hospital System, Roger C. Peace Rehabilitation Hospital, Greenville, SC
2004-2005	**Staff Physical Therapist**, Adult inpatient rehab/acute care, Good Samaritan Hospital, Cincinnati, OH
2006-2007, 2010	**Graduate Teaching Assistant**, Department of Physical Therapy, University of Florida, Gainesville, FL
2007-2009	**NIH T32 Predoctoral Fellow/Research Assistant**, Department of Physical Therapy, University of Florida, Gainesville, FL
2010	**Research Physical Therapist**, Department of Physical Therapy, University of Florida, Gainesville, FL
2010-pres.	**Adjunct Assistant Professor,** Department of Rehabilitation Sciences, University of Kentucky, Lexington, KY
2010-2012	**Research Scientist**, Cardinal Hill Rehabilitation Hospital, Lexington, KY
2011-2012	**Clinical Practice Director, Disorders of Consciousness Program (TBI Unit),** Cardinal Hill Rehabilitation Hospital, Lexington, KY
2012-2014	**Postdoctoral Research Fellow,** Moss Rehabilitation Research Institute, Philadelphia, PA
2013-pres.	**Assistant Professor,** Department of Physical Therapy, Arcadia University, Glenside, PA

Other positions:

2010-2012	Co-Chair, Research Committee, Cardinal Hill Rehabilitation Hospital
2010-2012	Clinical Practice Director, TBI Disorders of Consciousness Program Development Committee, Cardinal Hill Rehabilitation Hospital
2011-2012	Best Practice Committee, Cardinal Hill Rehabilitation Hospital
2011-2012	Research Committee, Physical Medicine and Rehabilitation Department of Research, University of Kentucky

2013-pres.	Disorders of Consciousness Task Force, Interdisciplinary Brain Injury SIG, American Congress of Rehabilitation Medicine
2013-pres.	Communications Task Force, Early Career Networking Group, American Congress of Rehabilitation Medicine
2013-pres.	Scholarship Task Force, Arcadia University Department of Physical Therapy

Honors:

1997-2000	Ohio University Dean's Scholarship
1997-1998	TriBeta National Biological Honorary, Ohio University
1997-1998	Alpha Lambda Delta Honor Society, Ohio University
1999-pres.	Phi Beta Kappa, Ohio University
1999-2000	Phi Kappa Phi Honor Society, Ohio University
1999-2001	Golden Key International Honour Society, Ohio University
1999-2000	Mortar Board Senior Honor Society, Ohio University
2000-2001	Office of Graduate Studies Scholarship, Ohio University
2001-2002	Cynthia Norkin Scholarship, Ohio University School of Physical Therapy
2004-2005	Service Excellence Award, Good Samaritan Hospital Rehab Dept.
2006	Grinter Fellowship, Dept. of Physical Therapy, University of Florida
2006	Outstanding Teaching Assistant Award, Department of Physical Therapy, University of Florida
2007-2009	NIH T32 Predoctoral Fellowship, "Interdisciplinary predoctoral training in neuromuscular plasticity and rehabilitation," University of Florida, Clinical Research Mentors: Andrea Behrman, PhD, PT, Steve Kautz, PhD, Basic Science Mentor: Dena Howland, PhD, OT
2007	Best Graduate Student Poster Presentation Award, Innovations in Balance and Locomotor Rehabilitation, International Society for Posture and Gait Research Preconference, Montreal, Canada
2009	Frederick Family Scholarship in Physical Therapy, Advanced Level Graduate Student Award, Department of Physical Therapy, University of Florida
2009-pres.	Neurologic Certified Specialist (NCS), American Board of Physical Therapy Specialties
2012	Professional Poster Presentation Award, Appalachian Health Summit/ Spring Neuroscience Day, Bluegrass Chapter of the Society for Neuroscience. Lexington, KY

C. Selected Peer-reviewed Publications

KV Day, SA Kautz, SS Wu, SP Suter, AL Behrman. Foot placement variability as a walking balance mechanism post-spinal cord injury. Clinical Biomechanics 2012 Feb;27(2):145-50. PMID: 22000699.

NJ Tester, DR Howland, **KV Day**, SP Suter, A Cantrell, AL Behrman. Device use, locomotor training, and the presence of arm swing during treadmill walking post-spinal cord injury. Spinal Cord 2011 Mar;49(3):451-6. PMID: 20938449.

MT Thigpen, J Cauraugh, G Creel, **K Day**, S Flynn, S Fritz, S Frost, R Respess, P Gardner-Smith, M Brack, A Behrman. Adaptation of postural responses during different standing perturbation conditions in individuals with incomplete spinal cord injury. Gait & Posture 2009 Jan;29(1):113-8. PMID: 18774296.

KV Day, SA Kautz, SP Suter, SS Wu, AL Behrman. Dynamic stability post-spinal cord injury: Differential effects of manual-assisted versus robotic-assisted locomotor training. *In Revisions, Journal of Rehabilitation Research and Development.*

KV Day, SA Kautz, SP Suter, SS Wu, AL Behrman. Influence of assistive devices on head stabilization during walking after spinal cord injury. *In Revisions. Journal of Applied Biomechanics.*

D. Ongoing Research Support:

Ellington Beavers Award for Intellectual Inquiry (Arcadia Univ)   Day (PI)   06/01/2014-05/31/2015
Examination of resting state EEG in persons with severe brain injury: neural mechanisms for the recovery of consciousness
This project aims to address the practical issues pertinent to acquisition of analyzable resting EEG data in persons with DoCs and to apply the refined methods in the assessment of whether shifts in EEG power and connectivity follow the same path as behavioral recovery.